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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/836,075	04/22/97	MAERTENS G	INNS:004/KAM

HM31/0323

PATRICIA A KAMMERER
ARNOLD WHITE & DURKEE
PO BOX 4433
HOUSTON TX 77210-4433

EXAMINER	
ZEMAN,M	
ART UNIT	**PAPER NUMBER**
1643	10

DATE MAILED: 03/23/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 12/29/97

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire -3- month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 63-73 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 63-73 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☒ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1643.

2. Claims 63-73 are pending in this application. Claims 1-62 have been canceled.

3. The election of Group I, corresponding to new claims 63-73, in the response filed 12/29/97, is acknowledged. The election of SEQ ID NOs: 1 and 2 as the elected species is also acknowledged.

Claim Rejections - 35 USC § 112

4. Claims 65-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 65 refers back to claim 63, which recites various subtypes of HCV, or their complements. In claim 65, the sequences are further defined by particular amino acid residues encoded by the sequences of claim 63. The complement of a sequence will not code for those amino acids.

Also in claim 65, as well as claims 66, 67, 69 and 73, a limitation requiring "at least one nucleotide differing from previously known HCV nucleotide sequences" is unclear. This

limitation may be read as requiring at least one additional mutation not described by the instant specification, or as having nucleotide changes as set forth in one of the identified sequences.

In claim 66, a "polynucleotide acid" is recited. It is not clear whether a polynucleotide or a polynucleic acid is intended, nor is there a definition of a polynucleotide acid present in the specification.

Claims 66 and 67 depend from any one of claims 63-65, and further recite that the polynucleic acid encodes the entire HCV polyprotein. Claim 64 does not recite sequences encoding the entire polyprotein of HCV. Claim 64 is limited to the listed short polynucleotide sequences from various regions and subtypes of HCV. Therefore claims 66 and 67 cannot properly depend from claim 64.

In claim 68, the phrase "which codes for the 5' UR" is indefinite, as an untranslated region, per definition, has no coding sequences. The phrase "which comprises 5' UR sequences" may be more definite.

In claims 69 and 73, the metes and bounds of the phrase "an analog thereof being homologous and biologically equivalent to said polypeptide" are unclear. The term analog can have several different meanings: a structural analog of a peptide may merely have the same 3-dimensional conformation, and no sequence relevance; a functional analog may have the same biological activity in one or more respects, but may be different in sequence or structure; an analogous protein may be a protein that is related in terms of evolution or sequence similarity; each of these meanings is distinct and could require chemical entities not disclosed by the instant

application. The term "homologous" is also unclear as it is not certain whether the polypeptide must be similar in structure, or sequence. If referring to the similarity between two sequences, the terms sequence similarity or sequence identity are preferred. The term "biologically equivalent" is unclear as none of the biological properties possessed by the polypeptides being claimed to which other polypeptides must be similar are set forth. There are innumerable biological properties which could fall within the scope of the claim, and it is not possible to determine which properties are relevant to the polypeptides being claimed, nor is it clear how similar the properties must be to be considered "equivalent".

Claim 70 recites the limitation "said insert" in reference to earlier steps in the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 63, 65-69 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by Qu et al..

Claims 63 and 65-68 recite polynucleotides which are unique to one of many subtypes of HCV. Claims 69 and 73 are drawn to polypeptides encoded by the nucleic acids of claims 63-65, or a part thereof. The species of SEQ ID NO: 1 was elected and all claims have been searched as far as they read upon that species. SEQ ID NO: 1 is a polynucleotide sequence which encodes the amino acid sequence of SEQ ID NO: 2. The specification sets forth at page 11 that sequences which are at least 90% identical at the nucleotide level, and at least 95% identical at the amino acid level to one another would be considered to be the same subtype.

Qu (Qu et al. 1994 J General Virology 75 (5) 1063-1070) discloses a polynucleotide sequence which has a greater that 91% sequence identity to SEQ ID NO: 1. (See the attached sequence alignment) This sequence therefore would be that of HCV subtype 1d. It is noted that SEQ ID NO: 1 has many "N" residues, meaning any nucleotide, and "K", "S" or "Y" residues designating two or more particular residues. In the alignment program, these are not counted as matches for the purpose of generating the query match percentage. If those residues are counted as being a proper match, the query match percentage would be approximately 95%. (an additional 14 bases would match) Qu indicates that the amino acid sequences were determined for these nucleic acid sequences. These polypeptides would satisfy the limitations of claims 69 and 73.

7. Claims 63, 65-69 and 73 are rejected under 35 U.S.C. 102(a) as being anticipated by JP 06-319563.

Okamoto (JP 06-319563) discloses an amino acid sequence having 99.5% identity to SEQ ID NO: 2 and nucleotide sequences encoding those polypeptides. (See attached sequence alignment) It is noted that SEQ ID NO: 2 has several "X" residues, meaning any amino acid. When those residues are counted as matches, the query match percentage increases. This sequence would therefore be that of HCV subtype 1d.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claim 64 is rejected under 35 U.S.C. 103(a) as being unpatentable over Qu or JP 06-319563.

Claim 64 is directed to particular SEQ ID NOs setting forth a portion of the subtype of HCV. Both Qu (Qu et al. 1994 J General Virology 75 (5) 1063-1070) and Okamoto (JP 06-319563) set forth sequences of the HCV 1d subtype. The existence of many subtypes of HCV was well known and discussed by both Qu and Okamoto. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have screened HCV positive donors for other sequences of the HCV 1d subtype, as it was well known that these sequences existed and it was expected that more sequences from various subtypes would be identified.

10. Claims 70-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Qu and Okamoto as applied to claims 63-69 and 73 above, further in view of Chien.

Claims 70-72 are drawn to recombinant production of HCV subtype polypeptides, as well as vectors and host cells for use in carrying out those methods.

Both Qu (Qu et al. 1994 J General Virology 75 (5) 1063-1070) and Okamoto (JP 06-319563) set forth sequences of the HCV 1d subtype. Chien (WO 93/00365) discloses methods of recombinantly expressing various epitopes of HCV, as well as vectors and host cells for use in those methods. Chien indicates that these methods can be used to express polypeptides from any subtype or type of HCV. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the sequences of Qu or Okamoto for the recombinant expression of polypeptide of new or different HCV subtypes, as those polypeptides would be useful diagnostic tools for the detection of HCV infection.

11. No claim is allowed.

The following documents were cited in the international search report, and are now made of record:

Liu et al. 1992 Gene 114 (2) 245-250

Stuyver et al. 1994 Journal of General Virology 74 (6) 1093-1102

Stuyver et al. 1994 PNAS USA 91 (21) 10134-10138

Van Doorn et al. 1994 Journal of Hepatology 21 (1) 122-129

WO 93/00365

WO 94/25601

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can be reached between the hours of 8:00 am and 5:30 pm Monday through Thursday, and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marian Knode, can be reached on (703) 308-4311.

The fax number for this Art Unit is (703) 305-7939.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

mkz
March 10, 1998

MICHAEL P. WOODWARD
PRIMARY EXAMINER
AU 1643